

### **REMARKS**

Claims 33 and 35-42 were pending. Applicants have herein canceled claim 42 without prejudice to their right to pursue the subject matter of this claim in another application, and amended claims 35-36. Entry of this amendment is respectfully requested such that claims 33 and 35-41 will be pending.

#### **Rejection under 35 USC 112, first paragraph**

The Office Action maintained the rejection under rejection under 35 USC 112, first paragraph and requested copies of the references cited in the declaration of Dr. Walter submitted in the prior response. During a conference call with the undersigned, Examiner Huff requested that applicants supply copies of the references such that she could more fully consider the declaration. Examiner Huff commented that supplying the references would constitute a fully responsive response to this ground of rejection. Applicants note that they have enclosed copies of the following references cited in the declaration:

Xiang J., Srivamadan, M., Rajala, R. and Jia, Z. (2000) Study of B72.3 combining sites by molecular modeling and site-directed mutagenesis. *Protein Eng* **13**, 339-344.

Hifumi, E., Okamoto, Y. and Uda, T. (2000) How and why 41S-2 antibody subunits acquire the ability to catalyze decomposition of the conserved sequence of gp41 of HIV-1. *Appl Biochem Biotechnol* **83**, 209-219; discussion 219-220, 297-313.

Demangel, C., Maroun, R.C., Rouyre, S., Bon, C., Mazie, J.C. and Choumet, V. (2000) Combining phage display and molecular modeling to map the epitope of a neutralizing antitoxin antibody. *Eur J Biochem* **267**, 2345-2353.

Luo, P., Canziani, G., Cunto-Amesty, G. and Kieber-Emmons, T. (2000) A molecular basis for functional peptide mimicry of a carbohydrate antigen. *J Biol Chem* **275**, 16146-16154.

Pitner, J.B., Beyer, W.F., Venetta, T.M., Nycz, C., Mitchell, M.J., Harris, S.L., Marino-Albernas, J.R., Auzanneau, F.I., Forooghian, F. and Pinto, B.M. (2000) Bivalency and epitope specificity of a high-affinity IgG3 monoclonal antibody to the Streptococcus group A carbohydrate antigen. Molecular modeling of a Fv fragment. *Carbohydr Res* **324**, 17-29.

Rognan, D., Engberg, J., Stryhn, A., Andersen, P.S. and Buus, S. (2000) Modeling the interactions of a peptide-major histocompatibility class I ligand with its receptors. II. Cross-reaction between a monoclonal antibody and two alpha beta T cell receptors. *J Comput Aided Mol Des* **14**, 71-82.

Raffai, R., Weisgraber, K.H., MacKenzie, R., Rupp, B., Rassart, E., Hiramata, T., Innerarity, T.L. and Milne, R. (2000) Binding of an antibody mimetic of the human low density lipoprotein receptor to apolipoprotein E is governed through electrostatic forces. Studies using site-directed mutagenesis and molecular modeling. *J Biol Chem* **275**, 7109-7116.

Muldoon, M.T., Holtzapfel, C.K., Deshpande, S.S., Beier, R.C. and Stanker, L.H. (2000) Development of a monoclonal antibody-based cELISA for the analysis of sulfadimethoxine. 1. Development and characterization of monoclonal antibodies and molecular modeling studies of antibody recognition. *J Agric Food Chem* **48**, 537-544.

Kleijung, J., Petit, M.C., Orlewski, P., Mamalaki, A., Tzartos, S.J., Tsikaris, V., Sakarellos-Daitsiotis, M., Sakarellos, C., Marraud, M. and Cung, M.T. (2000) The three-dimensional structure of the complex between an Fv antibody fragment and an analogue of the main immunogenic region of the acetylcholine receptor: a combined two-dimensional NMR, homology, and molecular modeling approach. *Biopolymers* **53**, 113-128.

Bernstein, F.C., Koetzle, T.F., Williams, G.J., Meyer, E.F., Jr., Brice, M.D., Rodgers, J.R., Kennard, O., Shimanouchi, T. and Tasumi, M. (1978) The protein data bank: a computer-based archival file for macromolecular structures. *Arch Biochem Biophys* **185**, 584-591.

Bohm, G. (1996) New approaches in molecular structure prediction. *Biophys Chem.* **59**, 1-32.

Burks, C., Fickett, J.W., Goad, W.B., Kanehisa, M., Lewitter, F.I., Rindone, W.P., Swindell, C.D., Tung, C.S. and Bilofsky, H.S. (1985) The GenBank nucleic acid sequence database. *Comput Appl Biosci* **1**, 225-233.

Eisenhaber, F., Persson, B., Argos, P. (1995) Protein structure prediction: recognition of primary, secondary, and tertiary structural features from amino acid sequence. *Crit Rev Biochem Mol Biol.* **30**, 1-94.

Greer, J. (1981) Comparative model-building of the mammalian serine proteases. *J Mol Biol*, **153**, 1027-1042.

Greer, J. (1990) Comparative modeling methods: application to the family of the mammalian serine proteases. *Proteins* **7**, 317-334.

Harris, L.J., Larson, S.B., Hasel, K.W., Day, J., Greenwood, A. and McPherson, A. (1992) The three-dimensional structure of an intact monoclonal antibody for canine lymphoma. *Nature* **360**, 369-372.

Iwahashi, M., Milenic, D.E., Padlan, E.A., Bei, R., Schlom, J. and Kashmiri, S.V. (1999) CDR substitutions of a humanized monoclonal antibody (CC49): contributions of individual CDRs to antigen binding and immunogenicity. *Mol Immunol* **36**, 1079-1091.

Johnson, V.G., Schlom, J., Paterson, A.J., Bennett, J., Magnani, J.L. and Colcher, D. (1986) Analysis of a human tumor-associated glycoprotein (TAG-72) identified by monoclonal antibody B72.3. *Cancer Res* **46**, 850-857.

Kashmiri, S.V., Shu, L., Padlan, E.A., Milenic, D.E., Schlom, J. and Hand, P.H. (1995) Generation, characterization, and in vivo studies of humanized anticarcinoma antibody CC49. *Hybridoma* **14**, 461-473.

Lin, L., Daugherty, B., Schlom, J., and Pestka, S. (1996) Construction of phosphorylatable monoclonal antibody to a tumor associated antigen. *Cancer Res.* **56**, 4250-4254.

Lin, L., Gillies, S.D., Schlom, J., and Pestka, S. (1998b) Construction of phosphorylatable chimeric monoclonal antibody CC49 with a tyrosine Src kinase recognition site. *Intl. J. Oncology* **13**, 725-732.

Moult, J. (1996) The current state of the art in protein structure prediction. *Curr Opin Biotechnol.* **7**, 422-427.

Moult, J. (1999) Predicting protein three-dimensional structure. *Curr Opin Biotechnol.* **10**, 583-588.

Padlan, E.A. (1994) Anatomy of the antibody molecule. *Mol Immunol* **31**, 169-217.

Reithmeier RA. (1995) Characterization and modeling of membrane proteins using sequence analysis. *Curr Opin Struct Biol.* **5**, 491-500.

Schott, M.E., Milenic, D.E., Yokota, T., Whitlow, M., Wood, J.F., Fordyce, W.A., Cheng, R.C. and Schlom, J. (1992) Differential metabolic patterns of iodinated versus radiometal chelated anticarcinoma single-chain Fv molecules. *Cancer Res* **52**, 6413-6417.

Slavin-Chiorini, D.C., Kashmiri, S.V., Schlom, J., Calvo, B., Shu, L.M., Schott, M.E., Milenic, D.E., Snoy, P., Carrasquillo, J., Anderson, K. and *et al.* (1995) Biological properties of chimeric domain-deleted anticarcinoma immunoglobulins. *Cancer Res* **55**, 5957s-5967s.

Tamura, M., Milenic, D.E., Iwahashi, M., Padlan, E., Schlom, J. and Kashmiri, S.V. (2000) Structural correlates of an anticarcinoma antibody: identification of specificity-determining residues (SDRs) and development of a minimally immunogenic antibody variant by retention of SDRs only. *J Immunol* **164**, 1432-1441.

Accordingly, applicants respectfully request full consideration of the declaration and reconsideration and withdrawal of this ground of rejection.

**Rejections under 35 USC 112, second paragraph**

The Office Action rejected the claims as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. With respect to claims 35 and 36, applicants have amended these claims such that they further limit claim 33. With respect to claim 42, applicants have canceled this claim without prejudice to their right to pursue the subject matter of this claim in another application. Accordingly, applicants respectfully request reconsideration and withdrawal of this ground of rejection.

**Rejections under 35 USC 112, first paragraph**

The Office Action rejected the claims as allegedly failing to comply with the written description requirement. In particular, the Office Action commented that the term "reduce" is not found in the specification. In response, applicants respectfully traverse and direct the Examiner's attention to, among other places, page 89, lines 20-23 which provides sufficient support. Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. PBLI-P01-007 from which the undersigned is authorized to draw.

Dated: January 13, 2006

Respectfully submitted,

By 

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